

AD \_\_\_\_\_

GRANT NUMBER DAMD17-98-1-8360

TITLE: Radiographic Density, Cancer, Inheritance and Acquired Risk in Twins

PRINCIPAL INVESTIGATOR: Thomas M. Mack, M.D.

CONTRACTING ORGANIZATION: University of Southern California  
Los Angeles, California 90033-0800

REPORT DATE: March 1999

TYPE OF REPORT: Final

PREPARED FOR: Commanding General  
U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20000828 222

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
<small>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.</small>				
1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE March 1999		3. REPORT TYPE AND DATES COVERED Final (15 Mar 98 14 Mar 99)
4. TITLE AND SUBTITLE Radiographic Density, Cancer, Inheritance and Acquired Risk in Twins			5. FUNDING NUMBERS DAMD17-98-1-8360	
6. AUTHOR(S) Thomas M. Mack, M.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Southern California Los Angeles, California 90033-0800			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) <p>Computerized mammographic density measurements have been linked to breast cancer risk; the greater the breast density, the higher the risk of breast cancer. Our goals are to confirm if these observations are true within pairs of identical twins, to determine the heritability mammographic density, and to determine if adult exposures and experiences related to breast cancer risk result in modifications of mammographic density. We are interviewing both members of up to 2500 twin pairs registered in the California Twin Program about the risk factors of interest, collecting mammograms from each twin, scanning the films and measuring the densities, and comparing the measurements between co-twins in light of zygosity, past experiences, and the appearance of subsequent breast cancer.</p> <p>Thus far we have identified 1922 potentially eligible individuals from 961 pairs, contacted 1255, and have obtained the cooperation of 1043 or 83%. We have received formal signed consents for (temporary) release of the mammograms from 806 twins, and have received and scanned 1319 of the 1364 mammograms from 646 of these, including both twins from 307 pairs. Cooperation from twins and their providers has been excellent. Results will not be available until blinded readings of the scanned films are available.</p>				
14. SUBJECT TERMS Breast Cancer			15. NUMBER OF PAGES 6	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

## FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

NA Where copyrighted material is quoted, permission has been obtained to use such material.

NA Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

NA Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

NA In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

NA For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

NA In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

NA In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

NA In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.



PI - Signature

Date

## **TABLE OF CONTENTS**

<b>INTRODUCTION</b>	<b>5</b>
<b>BODY</b>	<b>5</b>
<b>KEY RESEARCH ACCOMPLISHMENTS</b>	<b>5</b>
<b>REPORTABLE OUTCOMES</b>	<b>6</b>
<b>CONCLUSIONS</b>	<b>6</b>
<b>REFERENCES</b>	<b>6</b>
<b>APPENDICES</b>	<b>6</b>

## **INTRODUCTION**

Computerized mammographic density measurements have been linked to breast cancer risk; the greater the breast density, the higher the risk of breast cancer. Our goals are to confirm if these observations are true within pairs of identical twins, to determine the heritability of mammographic density by comparison of the similarity in density between the members of monozygotic and dizygotic twin pairs, and to determine if adult exposures and experiences related to breast cancer risk result in modifications of mammographic density by comparing the densities in exposed twins to the densities of their unexposed co-twins.

## **BODY**

There are no changes in the specific aims of the study. Until the stage of analysis, the workscope required by each of these three aims is identical, since all comparisons are between measures of mammographic density obtained after scanning the mammograms that have been obtained from the twins' providers. To maintain blind readings of the mammograms, it is preferable that neither breast cancer status, nor zygosity, nor history of breast cancer risk factors be available to the reader. Therefore the progress achieved is joint progress toward all aims.

## **KEY RESEARCH ACCOMPLISHMENTS**

- In the first year of the grant we developed and tested the interview instrument, and designed a tracking database for the purpose of following progress in the collection and review of mammograms from each eligible twin.
- At the completion of the first year we had contacted and obtained consent from the members of 347 pairs, but had not yet begun collection of mammograms, largely because the equipment requested was unavailable. That scanner and accompanying computer (the sole object of this DOD award) was received and put into operation, and additional personnel for purposes of interviewing have been engaged.
- To date we have generated contact forms (i.e. entered into the database) 1922 individuals representing 961 pairs
- Of these, we have contacted 1255 individuals, consisting of both twins from 569 pairs and 117 first-contacted individual twins. Of those, 1043 (83%) have agreed to participate, including both twins from 497 pairs. Twins from 14 pairs have been excluded on the basis of eligibility. Consent forms have been sent to 983 individuals and have been completed and returned by 806 individuals, including both members of 376 pairs.
- Mammograms were requested and received from 646 providers, including those from both members of 307 pairs. We have received and scanned 1319 of the 1364 mammograms from these 646 individuals.
- The protocol for scanning and assessing mammographic density has been adjusted. It has been decided that Dr. Ursin will herself read each of the scanned mammograms. We have had 2 visits from Martine Salane, each time serving to confirm readings by Dr. Ursine.
- We have had excellent cooperation, not only from twins, but from providers. No provider has refused cooperation, and only one (in New York state) refused to allow us to borrow the original mammogram, thus eliminating one pair. We have not lost track of a single film, although we did change carriers to Federal Express after concerns raised by some problems with the previous carrier.

### **REPORTABLE OUTCOMES**

The assemblage of the research resource described under the previous heading comprises a valuable research resource.

### **CONCLUSIONS**

None can be made until the final blind readings of the mammogram densities. There is every reason to believe that the results will provide a definitive answer to each of the questions posed by the goals, permitting mammography to be considered as a legitimate proxy outcome for purposes of short-term studies of intervention, and/or permitting mammographic density to be used as a practical quantitative guide to risk.

### **REFERENCES**

None

### **APPENDICES**

None